

or a salt thereof,

wherein

Y is lower alkylene;

R<sup>1</sup> is phenyl which is substituted with 1 or 2 same or different substituent(s) selected from the group consisting of halogen, lower alkyl, lower alkoxy, mono(or di or tri)halo(lower)alkyl, nitro, amino, lower alkylamino, di(lower)alkylamino, lower alkylthio, lower alkylsulfonyl, cyclo(lower)alkylsulfonyl, aminosulfonyl, lower alkylaminosulfonyl, di(lower)alkylaminosulfonyl, pyrrolidinylsulfonyl, morpholinylsulfonyl, pyrrolylsulfonyl, pyridylsulfonyl, pyrrolyl and pyridyl;

A<sub>1</sub> R<sup>2</sup> is phenyl which is substituted with hydroxy and a substituent selected from the group consisting of lower alkyl, mono(or di or tri) halo (lower) alkyl, mono (or di or tri)halo(lower)alkylsulfonyloxy, halogen, lower alkylenedioxy, lower alkoxy, lower alkoxycarbonyl, lower alkoxy(lower)alkoxy(lower)alkoxy, hydroxy, diphenyl(lower)alkylsilyloxy, tri(lower)alkylsilyloxy, hydroxy(lower)alkyl, cyano, amino, [mono(or di or tri)halo(lower)alkylcarbonyl]amino, lower alkylamino, N-(lower alkyl)-[mono(or di or tri)halo(lower)alkylcarbonyl]amino, pyrrolidinyl and morpholinyl which may be substituted with lower alkoxy(lower)alkyl or lower alkyl;

R<sup>3</sup> is hydrogen; and

R<sup>4</sup> is (2,6-dimethylmorpholino)(lower)alkyl; (3,3-dimethylmorpholino)(lower)alkyl; (cis-3,5-dimethylmorpholino)(lower)alkyl; ((3S,5S)-3,5-dimethylmorpholino)(lower)alkyl; ((3S,5R)-3,5-dimethylmorpholino)(lower)alkyl; (2-methoxymethylmorpholino)(lower)alkyl; (3-methoxymethylmorpholino)(lower)alkyl; (2-methoxymethyl-5-methylmorpholino)(lower)alkyl; (2-methoxymethyl-5,5-dimethylmorpholino)(lower)alkyl;

(3,5-dimethoxymethylmorpholino)(lower)alkyl; or (2,3-dimethoxymethylmorpholino)(lower)alkyl.

12. (New) The compound of claim 11, in which

Y is C<sub>1</sub>-C<sub>4</sub> alkylene;

R<sup>1</sup> is bis [mono (or di or tri) halo (C<sub>1</sub>-C<sub>4</sub>) alkyl] phenyl;

R<sup>2</sup> is phenyl which is substituted with hydroxy and a substituent(s) selected from the group consisting of C<sub>1</sub>-C<sub>4</sub> alkyl, mono (or di or tri) halo(C<sub>1</sub>-C<sub>4</sub>) alkyl, halogen, C<sub>1</sub>-C<sub>4</sub> alkoxy and hydroxy;

R<sup>3</sup> is hydrogen; and

R<sup>4</sup> is (2,6-dimethylmorpholino) (C<sub>1</sub>-C<sub>4</sub>) alkyl; (2-methoxymethylmorpholino) (C<sub>1</sub>-C<sub>4</sub>) alkyl; (3-methoxymethylmorpholino) (C<sub>1</sub>-C<sub>4</sub>) alkyl; or (2-methoxymethyl-5-methylmorpholino) (C<sub>1</sub>-C<sub>4</sub>) alkyl.

13. (Amended) The compound of claim 12, which is selected from the group consisting of

(1) 1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3-hydroxy-4-methylbenzyl)-4-[2-[(3R)-3-(methoxymethyl)morpholino]-ethyl]piperazine,

(2) 1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-(cis-2,6-dimethylmorpholino)ethyl]-2-(3-hydroxy-4-methylbenzyl)piperazine,

(3) 1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(3-hydroxy-4-methylbenzyl)-4-[2-[(2S,5S)-2-methoxymethyl-5-methylmorpholino]ethyl]piperazine,

(4) 1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)morpholino]ethyl]-2-(3-hydroxy-4-methylbenzyl)piperazine,

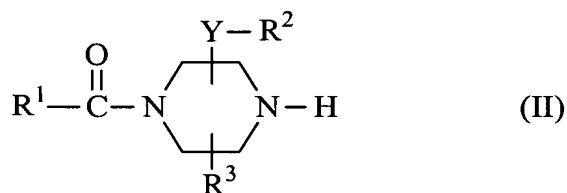
(5) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)morpholino]ethyl]-2-(3-hydroxy-4-methylbenzyl)piperazine, and

mo x  
F.P.  
(6) (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-2-(4-chloro-3-hydroxybenzyl)-4-[2-  
[(2S)-2-(methoxymethyl)morpholino]ethyl]piperazine,

or a pharmaceutically acceptable salt thereof.

14. (New) A process for the preparation of the compound, or a salt thereof, of claim 11, which comprises,

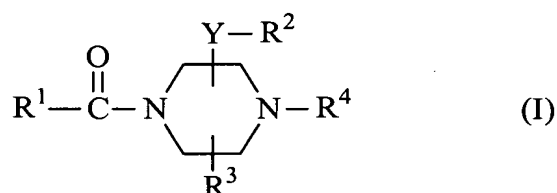
reacting a compound of the formula (II), or a salt thereof:



with a compound of the formula (III), or a salt thereof:



wherein  $\text{W}_1$  is a leaving group, to give a compound of the formula (I), or a salt thereof:



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^4$  and Y are each as defined in claim 11.

15. (New) A pharmaceutical composition which comprises, as an active ingredient, a compound of claim 11 or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutical acceptable carrier.

✓ 16. (New) A method for treating or preventing Tachykinin-mediated diseases of asthma, emesis, mental diseases, pollakiuria, urinary incontinence or irritable bowel syndrome, which comprises administering an effective amount of a compound, or a pharmaceutically acceptable salt thereof, of claim 11 to a human being or an animal.

A<sub>1</sub> 17. (New) The compound of claim 13, which is (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)morpholino]ethyl]-2-(3-hydroxy-4-methylbenzyl)piperazine, or a pharmaceutically acceptable salt thereof.

18. (New) The compound of claim 17, which is (2R)-1-[3,5-Bis(trifluoromethyl)benzoyl]-4-[2-[(2S)-2-(methoxymethyl)morpholino]ethyl]-2-(3-hydroxy-4-methylbenzyl)piperazine dihydrochloride.

---

#### DISCUSSION OF THE AMENDMENT

All of the claims have been cancelled and replaced with new Claims 11-18. Claim 11 is based on the combination of Claims 1 and 2, except that R<sup>2</sup> is substituted with two substituents, one of which must be hydroxy, R<sup>4</sup> omits 3-(3-pyridyl)propyl, 3-(3-pyridyl)propynyl, and 2-methoxymethylmorpholino(lower)alkenyl, and the proviso is omitted. Claim 12 is analogous to Claim 3, but has been made to be consistent with new Claim 11. Claim 13 is analogous to Claim 4, but omits compounds (4), (7), (9), and (10); the remaining compounds have been renumbered accordingly. Claim 14 is analogous to Claim 5, but is limited to reaction (1). Claim 15 is analogous to Claim 6. Claim 16 is analogous to Claim 8, but recites various diseases, as supported in the specification at page 21, line 30, through page 23, line 25. Claim 17 is supported by Claim 13. Claim 18 is supported in the specification, at page 46, lines 23-25, as the compound of Example 5 (1).